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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/884,715	06/19/2001	Malcolm Richard Boyd	4-31830B	3629

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
PENG, BO	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
01/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/884,715	BOYD, MALCOLM RICHARD	
	Examiner	Art Unit	
	Bo Peng	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/1/07 & 30 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 30, 2007, has been entered.

2. Claims 7-48 are pending and are considered in this Office action.

Allowable Subject Matter

3. The indicated allowability of Claims 7, 9, 10, 19, 20 23, 25, 26 and 46-48 is withdrawn after reconsideration of the teachings of the prior art.

35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. The rejection of Claims 8, 11, 12, 16-18, 21, 22, 24 and 27-45, under 35 U.S.C. 112, first paragraph, for failing to comply with the enablement requirement, **is withdrawn** in response to the amendment of the term "prophylaxis of HSV infection" to "prophylaxis of HSV-induced disease".

6. The rejection of Claims 13-15 under 35 U.S.C. 112, first paragraph, for failing to comply with the enablement requirement, **is maintained** because the term "prophylaxis of HSV infection" in Claims 13-15 remains unchanged. Therefore, the rejection of Claims 13-15 is maintained for the same reasons of record.

35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. The rejection of Claims 8, 11, 12, 16-18, 21, 24 and 27-34 under 35 U.S.C. 102(b) as being anticipated by Boker *et al*, **is maintained** and now extended to Claims 13-15 for the same reasons of record. Claims 35-45 are withdrawn from this rejection upon reconsidering the claim limitation.

9. Applicant argues that one patient studied in Boker *et al.* was not infected with herpes simplex virus; therefore, the patient was not treated for a HSV infection nor prophylactically treated for HSV-induced disease. The presently amended claims are therefore distinguished from the teaching of Boker *et al.*

10. Applicant's argument is considered but found not persuasive. To meet the claim requirement "prophylaxis of HSV-induced disease in a human in need", the patient population

can be anyone in need, including liver transplantation patients with previous HBV infection. Since immunosuppressed patients, like liver transplantation patients with previous HBV infection, are known to be at risk for newly-transmitted infections or reactivation of latent HSV infection, they meet the requirement for "prophylaxis of a HSV-induced disease in a human in need". Moreover, although Boker intends to reduce re-occurring of HBV in the liver transplant patient, HSV infections are also a complication found in liver transplant patients. See example of Ichai *et al* (Ichai *et al.* Liver Transpl 2005;11:1550-1555). Ichai *et al.* report that HSV superinfections occur in liver transplant patients with hepatitis B virus (HBV)-related chronic liver disease (Abstract, and p. 1553). HSV superinfection in these patients has significantly contributed to liver dysfunction aggravation and death. Ichai teaches that the diagnosis of HSV hepatitis is difficult due to lack of specific clinical sympotoms. Ichai *et al* suggest that early administration of antiviral treatment, like acyclovir, in patients with suspected HSV hepatitis is needed without waiting for virologic confirmation (Abstract).

11. For the reason discussed above, the method of prophylactic treatment of HBV in liver transplant patient taught in Boker reference inherently constitutes "prophylaxis of HSV-induced disease in a human in need", even though the reference is silent upon the topic of herpes viruses. Thus, the alleged method of Claims 8, 11-18, 21, 24 and 27-34 as amended does not distinguished from the teaching of Boker. The rejection therefore is maintained.

13. Following are new ground of rejections:

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 7-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Field *et al* (Antimicrobial Agents and Chemotherapy 39:11114-1119, 1995 or Antiviral Chemistry & Chemotherapy 6:210-216, 1995), and Harrell *et al* (Drug Metab Dispos. 1993; 21(1):18-23).

16. **Claims 7, 9, 10, 19, 20, 23, 25, 26 and 46-48** are directed to a pharmaceutical composition for oral or parenteral administration comprising a nucleoside analogue active against herpes simplex virus selected from the group consisting of penciclovir (PCV) and famciclovir (FCV), and an effective amount of a pharmaceutically acceptable immunosuppressant, wherein the immunosuppressant is selected from the group consisting of a cytotoxic agent, a corticosteroid and a non-steroidal anti-inflammatory agent, wherein the immunosuppressant is selected from the group consisting of cyclophosphamide, cyclosporine A (CyA), hydrocortisone, and dexamethasone. **Claims 8, 11-18, 21, 22, 24, 27-45** are directed to a method of treatment of herpes simplex virus (HSV) infections or prophylaxis of HSV-induced disease in a human in need thereof, which method comprises administering orally or parenterally, to said human, an effective amount of a nucleoside analogue active against HSV selected from the group consisting of penciclovir and famciclovir, and a pharmaceutically acceptable immunosuppressant, wherein the immunosuppressant is selected from the group

consisting of a cytotoxic agent, a corticosteroid and a non-steroidal anti-inflammatory agent, wherein the immunosuppressant is selected from the group consisting of cyclophosphamide, cyclosporine A, hydrocortisone, and dexamethasone, wherein the PCVand FCV, and immunosuppressants are administered simultaneously, separately or sequentially.

17. Field provides teaching indicating a method of treating HSV infection by oral or parenteral administration of a nucleoside analogue, specifically FCV, and immunosuppressant, such as CyA, wherein the FCV and CyA may be administered simultaneously, separately or sequentially (Para 2-4, left col. p. 1115). Specifically, Field teaches in a HSV infected mouse model that FCV is administered orally to mice **daily** on day 5 or 10 post inoculation, CyA is administered by subcutaneous (s.c.) injection on **alternate days** at day 0, 2, 4, 6, 8 and 10 (Para 2-4, left col. p. 1115). Field teaches that in FCV- and CyA-treated mice, FCV is remarkably effective in preventing the development of clinical symptoms and viral clearance from the tissue, resulting no recurrence of viral infection (Abstract, p. 1116 and 1117, Table 2 and Figures 2-4).

18. Field also provides teachings indicating that CyA and FCV may be administered together without adverse drug-drug interaction. Field teaches that the co-administration of FCV and CyA does not affect the immunosuppressive effect of CyA, and CyA treatment does not alter the absorption or metabolism of FCV (Para 1, left col. p. 1117).

19. Field teaches that the mouse model of HSV-1 infection is developed as an immunocompromised host for studying the efficacy of antiviral drugs against clinical disease and virus replication in tissue local to the inoculation site and in the central nervous system (Para 1, right col. p.1114, and Abstract).

20. Field does not teach treating HSV in humans using FCV and CyA. Field does not explicitly teach a pharmaceutical composition **consisting of** penciclovir and FCV and CyA.

21. Harrell suggests co-administration of FCV and CyA for combating herpes viral infections in humans after organ or bone marrow transplants (Abstract, and right col. p. 18). Harrell teaches that famciclovir and penciclovir can be co-administered with CyA because FCV and PCV do not affect a human enzyme which acts on CyA.

22. In view of these teachings, it would also have been obvious to one of ordinary skill in the art at the time the invention was made to administer both an immunosuppressant, such as CyA, and FCV or its metabolite penciclovir, in effective amounts for treatment of an HSV infection in patients in need, as taught by Field. The skilled artisan would have been motivated to do so and have a reasonable expectation of success for treating HSV infection in a patient in need, given that co-administering FCV and CyA is remarkably effective in preventing the development of clinical signs, clearing virus from the tissue, and preventing recurrence of viral infection in the mouse model of HSV-1 infection, and also given that the mouse model of HSV-1 infection is recognized as an acceptable animal model for studying efficacy of antiviral drugs in an immunocompromised host, as taught by Field.

23. It would also have been obvious to one of ordinary skill in the art at the time the invention was made to combine the drugs FCV and CyA into a single composition for treating HSV infections in humans in need, such as immunocompromised individuals, as suggested by Harrell. The skilled artisan would have been motivated to do so and would have been a reasonable expectation of success, given the suggestion by Harrell that co-administration of

famciclovir and CyA for combating herpes viral infections in humans after organ or bone marrow transplants, and also given the knowledge that co-administration of famciclovir and penciclovir with CyA does not result in a drug-drug interaction as taught by Harrell and Field. Thus, the invention as a whole is seen as *prima facie* obvious, absent unexpected results.

Double Patenting

24. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

25. Claims 7-48 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-16 of copending Application No. 11/105,842 ('842). Although the conflicting claims are not identical, they are not patentably distinct from each other because Claims 7-48 of the instant application is obvious variation of the invention defined in the co-pending application '842. Claims 1-16 of '842 encompass all routes

of administration, including oral or parenteral route, which clearly cover the limitation of oral or parenteral route of administration recited in Claims 7-48 of the instant application. Therefor, the instant invention is obvious variation of the invention defined in the co-pending application '842.

26. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Remarks

27. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on M-F, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, Ph.D. can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Bo Peng/
Patent Examiner
December 26, 2007